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| 09/724,319 | 11/27/2000 | Dale B. Schenk | 15270J-004743US | 6653 |

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| EXAMINER | |
|---|---|
| KOLKER, DANIEL E | |

| ART UNIT | PAPER NUMBER |
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| 1649 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/724,319 | SCHENK, DALE B. | |
| | Examiner | Art Unit | |
| | Daniel Kolker | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-58,61,63-66,71-79,81,85,86,92-94,97,99,164-191,194-205 and 207-209* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/19/07; 10/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 56-58,61,63-66,71-79,81,85,86,92-94,97,99,164-191,194-205 and 207-209.

## DETAILED ACTION

1. The remarks, amendments, and declaration filed 23 October 2007 have been entered. Claims 56 – 58, 61, 63 – 66, 71 - 79, 81, 85 - 86, 92 - 94, 97, 99, 164 - 191, 194 - 205, and 207 - 209 are pending and under examination.

### *Withdrawn Rejections and Objections*

2. The following rejections and objections set forth in the previous office action are withdrawn:

A. The objection to claim 57 is withdrawn in light of the amendments suggested by the examiner.

B. The rejection under 35 USC 112, first paragraph, is withdrawn in light of the arguments. At p. 11 of the remarks filed 23 October 2007, applicant persuasively argues that the post-filing publications provide evidence that the claimed invention is effective as described in the publication.

C. The rejections under 35 USC 102(e) and 35 USC 103(a) over Solomon (U.S. Patent 5,688,651) is withdrawn in light of the arguments and declaration. The declaration under 37 CFR 1.132 filed 23 October 2007 is sufficient to overcome the rejections based upon the evidence set forth in the declaration which indicates that antibody AMY-33 from the Solomon reference does not bind to residues 13-28 of Aβ. As the declaration provides evidence that the antibody from Solomon is beyond the scope of the independent claims, the rejections are withdrawn.

### *Information Disclosure Statement*

3. The IDS filed 19 July 2007 has been considered. References 790 (by Bales), 793 (by Zameer) and 838 have been crossed off. No date has been supplied, and the examiner cannot determine if these references are prior art.

### *Maintained Rejections and Objections*

#### *Priority*

4. The effective filing date for all pending claims is 7 April 1998 for the reasons previously made of record. Applicant did not traverse the examiner's determination that this is the appropriate effective filing date.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 56 – 58, 61, 63, 64 – 66, 71 - 79, 81, 85 - 86, 92 - 94, 97, 99, 164 - 191, 194 - 205, and 207 – 209 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson (U.S. Patent 5,589,154, of record), in view of Becker (EP 613007, of record) and Schenk (U.S. Patent 5,593,846, of record).

This rejections is maintained for the reasons of record with respect to claims 97, 99, and 164 - 182. The reasons why the limitations of each of claims 97, 99, and 164 – 182 are met by the references are set forth in the previous office action and for the sake of brevity will not be reiterated here. Applicant did not traverse the examiner's determination that the specific limitations recited in claims 164 – 182 would have been obvious to one of ordinary skill in the art, but rather addressed the obviousness of selecting antibody 266. The examiner has also included claims 56 – 58, 61, 63, 64 – 66, 71 - 79, 81, 85 - 86, 92 - 94, drawn to treatment of Alzheimer's disease in patients having the disease, and claims 183 – 191, 194 – 205, and 207 – 209, drawn to reducing the risk or delaying the onset of disease in patients at risk of the disease, for the reasons set forth below. It is noted that the limitations in these claims also appear in claims 99 and 164 – 182. As the obvious features of these claims have been addressed by the examiner and not traversed by applicant, the claims which are drawn to the same features but depend from independent claims 56 and 183 respectively are included in this rejection.

Anderson teaches administration of antibodies against Aβ for diagnosis of Alzheimer's disease (see paragraph spanning columns 4-5 as well as column 12 final paragraph – column 13 line 45). The reference is on point to claim 97, drawn to pharmaceutical compositions, and claim 183, which encompasses administration to patients who do not have Alzheimer's. Anderson discloses that where chronic or prolonged administration is desired, the use of non-immunogenic antibodies is preferred, such as humanized antibodies (see column 12, lines 10-

25). Anderson teaches that either in vivo or in vitro methods can be used; see column 13 lines 33 – 45). Anderson also teaches pharmaceutically useful compositions, wherein the antibody or other agent is combined in admixture with a pharmaceutically acceptable carrier vehicle (see column 16, lines 8-11). As patients who display some symptoms of disease but do not yet have the disease are those in need of diagnosis, the reference by Anderson is on point to claims 183 – 186, 189 – 191, 194 – 203, and 207 – 209. However Anderson does not explicitly teach antibodies that bind to epitopes within residues 13 – 28 of Aβ as recited in independent claims 56, 97, and 183, and does not explicitly teach antibodies that either are humanized monoclonal 266 or compete with antibody 266.

Becker teaches the use of anti-Aβ antibodies for both *in vitro* and *in vivo* diagnosis of disease states or biological status in mammals, preferably humans (see column 7, lines 39-44). Becker teaches that the disclosed antibodies include humanized and human antibodies (see column 5, line 51 – column 6, line 21). Becker specifically teaches that when antibodies are administered to humans, care should be taken to humanize the antibodies to make them less immunogenic (see column 6 lines 31 - 53). Becker also discloses pharmaceutical formulations for parenteral administration containing the anti-Aβ antibodies, which is on point to claim 97, as well as products for parenteral administration formulated and distributed in solid, preferably freeze-dried form, for reconstitution immediately before use. Becker also teaches that the antibodies disclosed in the invention are to be used in diagnosis and treatment of patients suffering from Alzheimer's disease (see column 7 lines 39 – 52 and column 8 lines 16 – 18). As Becker teaches treatment of humans having Alzheimer's disease by administration of antibodies against Aβ, the reference is on point to instant claims 58, 61, 63, 64 – 66, 71 - 79, 81, 85 - 86, 92 - 94. Additionally, as patients with Alzheimer's disease are encompassed by claim 183, and Becker teaches treatment by administering the antibodies, delay of onset of more severe symptoms of the disease would necessarily happen upon administration. Thus the reference by Becker is also on point to claims 183 – 186, 189 – 191, 194 – 203, and 207 – 209. However Becker does not explicitly teach antibodies that bind to epitopes within residues 13 – 28 of Aβ as recited in independent claims 56, 97, and 183, and does not explicitly teach antibodies that either are humanized monoclonal 266 or compete with antibody 266.

Schenk teaches that antibodies which recognize residues 13-28 of Aβ are useful for the detection of Aβ because they are not cross-reactive with the larger amyloid precursor protein

(APP) from which Aβ is derived. Schenk teaches that one such antibody, referred to as 266, is particularly useful as a diagnostic, and provides evidence that the antibody can be used to distinguish those patients with Alzheimer's disease from those that do not have it (see for example column 17 line 50 – column 18 line 44 as well as Figures 2 – 3). Schenk explicitly teaches *in vivo* administration of the antibodies for detection of the disease (see column 10 lines 6 – 9), which is on point to claims 56, 97, and 183. However Schenk does not teach humanizing the antibody as encompassed by independent claims 56, 97, and 183.

It would have been obvious to one of ordinary skill in the art to select antibody 266, taught by Schenk, for use in the in vivo diagnostic assays of Becker and Anderson. Additionally, it would have been obvious to one of ordinary skill in the art to humanize the antibody, as suggested by Becker and by Anderson, when administering to human patients. Therefore, the invention encompassed by claims 56 – 58, 61, 63, 64 – 66, 71 - 79, 81, 85 - 86, 92 - 94, 97, 99, 164 - 191, 194 - 205, and 207 – 209 would have been obvious to one of ordinary skill in the art.

On pp. 13 – 14 of the remarks filed 23 October 2007, applicant traverses the rejection as it applied to claims 97, 99, and 164 – 182. Specifically, applicant argues that 1) Schenk does not teach in vivo assays but rather in vitro assays on bodily fluids and therefore the reference is not analogous prior art, and 2) the artisan of ordinary skill would not have been motivated to select antibody 266 for use in the assays of Becker or Anderson. Applicant's arguments have been fully considered but they are not persuasive.

With respect to 1), applicant points out that following the mention of in vivo diagnostic assays, Schenk '846 patent discusses certain in vitro assays on body fluids. The examiner notes that while this is the case, as the term "in vivo" does not have an explicit definition in the '846 patent, the examiner must rely on the term's plain meaning. "In vivo" refers to events happening within, or drugs administered to, living beings. The plain meaning of the term is not analysis of body fluids in a laboratory. While that is one interpretation of "in vitro", Schenk '846 clearly states that 266 antibody is to be used for diagnosis in vivo (see column 10 lines 6 – 9).

With respect to 2), applicant argues that since 266 antibody has little if any propensity to bind Aβ plaques, the artisan of ordinary skill would not have been motivated to select the antibody. Applicant pointed to a section of the instant application and a post-filing reference in support of this finding. However both the instant application and the post-filing reference, even if they do teach away from the efficacy of 266, would not have been available to the artisan of

ordinary skill at the time the invention was made. Furthermore, the Schenk '846 patent points to the usefulness of 266 antibody in diagnostic assays beyond any ability to bind to plaques. In the abstract, and at column 4 lines 39 – 55, Schenk discusses how 266 antibody is useful in detecting soluble Aβ. Thus the artisan of ordinary skill would have been motivated to select 266 antibody for use as an in vivo diagnostic in the methods of Becker or Anderson, as Schenk discusses the ability of this antibody to distinguish patients with Alzheimer's from those who do not have the disease.

***New Rejections***

***Double Patenting***

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 97 and 164 – 182 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 164, 168, 173, 175 –

197, 201, 208 – 217, 220 – 229 of copending Application No. 10/923474. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '474, which encompass humanized antibodies that to residues 15 – 20 of Aβ, anticipate the instant claims. The claims in the '474 application are species in that the epitope recited is entirely within that recited in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 56 – 58, 61, 63 - 66, 71 – 79, 85 – 86, and 92 – 94 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 164 - 229 of copending Application No. 10/923469. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims encompass methods of treating Alzheimer's by administering humanized antibodies that bind to residues 13 – 28 of Aβ (see for example claims 164 and 165 of '469 application).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 97, 99, and 164 – 182 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 164 – 166, 168 – 179, 185, and 187 - 193 of copending Application No. 10/923471. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims encompass products comprising humanized monoclonal 266 antibody. While the instant claims are drawn to pharmaceutical compositions rather than the antibodies themselves, addition of a pharmaceutically acceptable carrier would have been obvious to one of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
January 3, 2008

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER